

General

Guideline Title

Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer.

Bibliographic Source(s)

Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, Klimberg S, Chavez-MacGregor M, Freedman G, Houssami N, Johnson PL, Morrow M, Society of Surgical Oncology, American Society for Radiation Oncology. Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *J Clin Oncol*. 2014 May 10;32(14):1507–15. [PubMed](#)

Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, Klimberg S, Chavez-MacGregor M, Freedman G, Houssami N, Johnson PL, Morrow M. Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *Ann Surg Oncol*. 2014 Mar;21(3):704–16. [PubMed](#)

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Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

1. Positive Margins

A positive margin, defined as ink on invasive cancer or ductal carcinoma in situ (DCIS), is associated with at least a 2-fold increase in ipsilateral breast tumor recurrence (IBTR). This increased risk in IBTR is not nullified by:

- Delivery of a boost dose of radiation
- Delivery of systemic therapy (endocrine therapy, chemotherapy, or biologic therapy), or
- Favorable biology

2. Negative Margin Widths

Negative margins (no ink on tumor) minimize the risk of IBTR. Wider margin widths do not significantly lower this risk. The routine practice

to obtain negative margin widths wider than no ink on tumor is not indicated.

3. Systemic Therapy

The rates of IBTR are reduced with the use of systemic therapy. In the uncommon circumstance of a patient not receiving adjuvant systemic therapy, there is no evidence suggesting that margins wider than no ink on tumor are needed.

4. Biologic Subtypes

Margins wider than no ink on tumor are not indicated based on biologic subtype.

5. Radiation Therapy Delivery

The choice of whole-breast radiation therapy (WBRT) delivery technique, fractionation, and boost dose should not be dependent on margin width.

6. Invasive Lobular Carcinoma and Lobular Carcinoma in situ

Wider negative margins than no ink on tumor are not indicated for invasive lobular carcinoma (ILC). Classic lobular carcinoma in situ (LCIS) at the margin is not an indication for re-excision. The significance of pleomorphic LCIS at the margin is uncertain.

7. Young Age

Young age (≤ 40 years) is associated with both increased IBTR after breast-conserving therapy (BCT) as well as increased local relapse on the chest wall after mastectomy, and is also more frequently associated with adverse biologic and pathologic features. There is no evidence that increased margin width nullifies the increased risk of IBTR in young patients.

8. Extensive Intraductal Component

Extensive intraductal component (EIC) identifies patients who may have a large residual DCIS burden after lumpectomy. There is no evidence of an association between increased risk of IBTR and EIC when margins are negative.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Stages I and II invasive breast cancer

Guideline Category

Management

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Pathology

Radiation Oncology

Surgery

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To examine the relationship between margin width and ipsilateral breast tumor recurrence (IBTR) and develop a guideline for defining adequate margins in the setting of breast conserving surgery and adjuvant radiation therapy
- To assist treating physicians and patients in the clinical decision-making process

Target Population

Women who have undergone breast-conserving surgery and adjuvant radiation therapy for stages I and II invasive breast cancer

Interventions and Practices Considered

1. Use of established positive and negative margin widths to minimize ipsilateral breast tumor recurrence (IBTR) risk
2. Systematic therapy
3. Consideration that margin widths have no association with biologic subtypes, radiation therapy delivery, invasive lobular carcinoma (ILC), lobular carcinoma in situ (LCIS) or age

Major Outcomes Considered

- Risk of ipsilateral breast tumor recurrence (IBTR)
- IBTR rate
- Margin width
- Local failure

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Review and Meta-analysis

A comprehensive literature search of MEDLINE and evidence-based medicine was conducted of articles published from 1965 to January 2013, and was combined with data from a previously published systematic review that included 21 studies from 1965 to 2010. These new analyses are referred to as the margins meta-analysis and are part of the work led by Houssami et al., (see the "Availability of Companion Documents" field).

Inclusion/Exclusion Criteria

Studies eligible for inclusion had to allow for calculation of the proportion of ipsilateral breast tumor recurrence (IBTR) in relation to margin widths and had to meet the following criteria: (1) patients had to have early-stage invasive breast cancer (BC) (stages I and II); patients treated with neoadjuvant chemotherapy or with pure ductal carcinoma in situ were not included; (2) treatment consisted of breast-conserving therapy (BCT)

(all patients receiving adjuvant whole-breast radiation therapy [WBRT]); (3) microscopic margins had to be reported quantitatively with defined threshold distances/widths; (4) age data had to be present; and (5) a minimum median/mean follow-up time of 4 years was required. Details of the data collected can be found in the complete publication of the meta-analysis and are included in Supplementary Appendix A (see the "Availability of Companion Documents" field).

Number of Source Documents

The margins meta-analysis was based on 33 eligible studies.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The systematic review methods were adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations, Institute of Medicine (IOM) standards for systematic reviews and meta-analyses, and previously published methods.

All studies eligible for inclusion in the margins meta-analysis were reviewed and underwent data extraction by 2 independent investigators as described elsewhere. A study-level analysis was conducted, and was adjusted for study-specific median follow-up time (to account for the inherent increased risk of ipsilateral breast tumor recurrence [IBTR] with longer follow-up) as well as co-variates.

Study Quality and Limitations of the Literature

All publications that met the inclusion criteria were retrospective in nature, with the exception of 2 studies. Therefore, the majority of studies included in the meta-analysis provided observational-level data, and the analysis was conducted at the study level because of a lack of patient-level data from the retrospective studies. The characteristics and quality assessment of the studies included in the meta-analysis are reported in Houssami et al., (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Society of Surgical Oncology (SSO) and American Society for Radiation Oncology (ASTRO) convened a multidisciplinary expert panel (i.e., Margins Panel [MP]) in 2013 for the purpose of examining the relationship between margin width and ipsilateral breast tumor recurrence (IBTR). The primary clinical question was: What margin width minimizes the risk of IBTR? Specific clinical circumstances that might have an impact on this question, such as tumor histology, patient age, use of systemic therapy, and technique of radiation delivery, were also examined.

The MP comprised a multidisciplinary group of experts designated by their respective organizations, an expert methodologist who led the evidence review, and a patient representative (see Table 2 in the original guideline document). The process for development of this guideline followed, to the extent possible, the standards of the Institute of Medicine (IOM). The panel commissioned a systematic review and meta-analysis of the literature as the primary evidence base for the guideline. Additional literature reviews for specific clinical questions that could not be addressed in the meta-analysis were performed by designated panel members. The panelists met in July 2013, and all of the recommendations in this guideline were unanimously adopted.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline manuscript was approved by all panel members and sent to external reviewers for feedback, which was incorporated into the final document. The content of the manuscript was approved by the Society of Surgical Oncology (SSO) Executive Council and American Society for Radiation Oncology (ASTRO) Board of Directors.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence for each recommendation is listed in Table 1 in the original guideline document. In general, the majority of the evidence was obtained from retrospective studies and meta-analysis of observational-level data.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved clinical decision-making for patients and physicians when defining adequate margins in the setting of breast conserving surgery and adjuvant radiation therapy
- The use of no ink on tumor (negative margins) as the standard for an adequate margin in invasive cancer in the era of multidisciplinary therapy is associated with low rates of ipsilateral breast tumor recurrence (IBTR) and has the potential to decrease re-excision rates, improve cosmetic outcomes, and decrease health care costs.

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

- This guideline presents scientific, health, and safety information and reflects scientific or medical opinion interpreting that information. It is made available to Society members and to the public for educational and informational purposes only. Any commercial use of any content in this guideline without the prior written consent of the American Society of Radiation Oncology (ASTRO) and the Society of Surgical Oncology (SSO) is strictly prohibited.
- Adherence to this guideline will not ensure successful treatment in every situation. Furthermore, this guideline should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding the propriety of any specific therapy must be made by the physician and the patient in light of all circumstances presented by the individual patient. ASTRO and SSO assume no liability for the information, conclusions, and findings contained in this guideline.
- In addition, this guideline cannot be assumed to apply to the use of these interventions performed in the context of clinical trials, given that clinical studies are designed to evaluate or validate innovative approaches in a disease for which improved staging and treatment are needed or are being explored. This guideline was prepared on the basis of information available at the time the panel was conducting its research and discussions on this topic. There may be new developments that are not reflected in this guideline, and that may, over time, be a basis for ASTRO and SSO to consider revisiting and updating the guideline.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Mar 1

Guideline Developer(s)

American Society for Radiation Oncology - Professional Association

Society of Surgical Oncology - Medical Specialty Society

Source(s) of Funding

Supported by a grant from Susan G. Komen.

Guideline Committee

Margins Panel

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the time of the initial telephone planning conference, the Margins Panel (MP) candidates declared and discussed their potential conflicts. Written disclosures were subsequently obtained at the consensus meeting. The co-chairs reviewed each conflict of interest (COI) form and determined that there were no individuals on the panel for whom a COI could influence the development or process of specific recommendations for this guideline.

Guideline Endorser(s)

American Society of Breast Surgeons - Professional Association

American Society of Clinical Oncology - Medical Specialty Society

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [International Journal of Radiation Oncology Biology Physics Web site](#) , the [Journal of Clinical Oncology Web site](#) , and the [Annals of Surgical Oncology Web site](#) .

Availability of Companion Documents

The following are available:

- Society of Surgical Oncology–American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. Supplementary Appendix A. 2014. 5 p. Electronic copies: Available from the [International Journal of Radiation Oncology Biology Physics Web site](#) .
- Houssami N, Macaskill P, Marinovich ML, Morrow M. The association of surgical margins and local recurrence in women with early stage invasive breast cancer treated with breast conserving therapy: a meta-analysis. *Ann Surg Oncol*. 2014 Mar;21(3):717–730. Electronic copies: Available from the [Annals of Surgical Oncology Web site](#) .
- Buchholz TA, Somerfield MR, Griggs JJ, El-Eid S, Hammond ME, Lyman GH, Mason G, Newman LA. Margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer: American Society of Clinical Oncology endorsement of the Society of Surgical Oncology/American Society for Radiation Oncology consensus guideline. *J Clin Oncol*. 2014 May 10;32(14):1502–1507. Electronic copies: Available from the [Journal of Clinical Oncology Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 2, 2014. The information was verified by the guideline developer on July 31, 2014.

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